

REMARKS

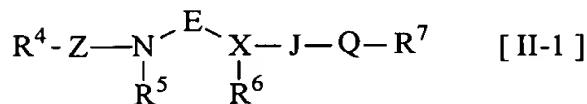
Claims 4-8, 13, 14, 22, 27, 28, 31-34, and 36-54 are active in the present application.

Applicants wish to thank Examiner Covington for the helpful and courteous discussion with their undersigned Representative on January 14, 2003. In addition, Applicants wish to thank Examiner Covington for the suggestions to avoid possible rejections under 35 U.S.C. §112. The content of this discussion is expanded upon herein below.

The rejection of Claims 1-14, 22-34, and 36-38 under 35 U.S.C. §102(b) over Oku et al (listed as U.S. 5,256,528, but believed to be U.S. 5,250,528) is obviated in part by amendment and traversed in part.

The present invention, as set forth in the independent Claims 4 and 5, provides an agent for expression of long-term potentiation of synaptic transmission comprising a compound having the following formula [II-1] (see Claim 4) or [II-2] (see Claim 5) or pharmaceutically acceptable salts thereof.

The compound of formula [II-1] is defined as:



wherein

R^4 is acyl,

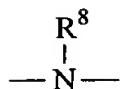
R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino, cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, -CO- or -SO₂-,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R⁸ is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is -CH₂-, -CO-, -SO₂- or -N=CH-, and

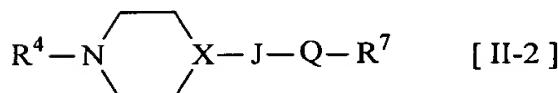
R⁵ and R⁶ are each hydrogen, lower alkyl, are taken together to form lower alkylene or are taken together to form lower alkylene condensed with a cyclic hydrocarbon or a heterocyclic ring,

provided that when X is N,

then 1) J is a single bond, and Q is -CH₂-, -CO- or -SO₂-, or

2) J is lower alkylene (see Claim 4).

The compound of formula [II-2] is defined as:



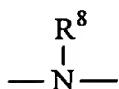
wherein

R⁴ is acyl,

R⁷ is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or

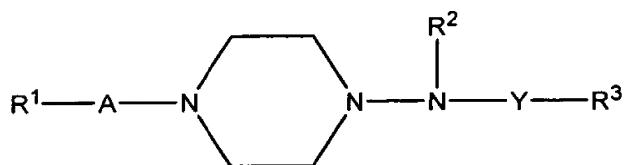


wherein R⁸ is hydrogen, lower alkyl or an N-protective group,

Q is -CH₂-, -CO- or -SO₂-,

provided that when X is N, then J is a single bond or lower alkylene (see Claim 5).

Inspection of the two compounds above reveals that when a piperazine group is present in the compound, the nitrogen at positions 1 and 4 may not be directly adjacent to another nitrogen atom. This is in direct contrast to the compound disclosed by Oku et al, which has the 1-nitrogen adjacent to another nitrogen. For the Examiner's convenience the general structure from Oku et al is reproduced below (see Abstract):



The standard for determining anticipation requires that the reference "must teach every element of the claim" (MPEP §2131). Therefore, the absence of any disclosure or suggestion in Oku et al of any compound having the following formula [II-1] (see Claim 4) or [II-2] (see Claim 5) would necessarily make these references fail to anticipate the present invention set forth in Claims 4 and 5 and all claims dependent therefrom.

Applicants request withdrawal of this ground of rejection.

The objection to the specification for failure to include an abstract is obviated by the submission of a substitute Abstract herewith. Withdrawal of this objection is requested.

On page 3, line 12 of paper number 7, the Examiner indicates that the "pre-amendment of 11/28/01 has not been entered because it is unclear." However, as evidenced by the enclosed copy of the date-stamped filing receipt from November 28, 2001, a preliminary amendment was not filed on this date. In fact, the only preliminary amendment

filed in this application was on March 14, 2002 (see attached copy of the date-stamped filing receipt). Applicants request further clarification from the Examiner to ensure that all amendments filed have been acted upon appropriately and that the record clearly reflects the amendments presented therein. If additional information is required from Applicants, they request that the Examiner contact their undersigned Representative without delay.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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Docket No.: 215869US0PCT
Serial No.: 09/926,641

MARKED-UP COPY

IN THE ABSTRACT OF THE DISCLOSURE

Please cancel the original Abstract appearing on page 76 and insert therefor the substitute Abstract submitted herewith as new page 76.

IN THE SPECIFICATION

Please insert the following text at page 1, line 1:

CROSS REFERENCE TO RELATED CASES

The present application is a 371 application of PCT/JP00/03334, filed on May 24, 2000, which is a continuation application of U.S. Application Serial No. 09/321,745 (now U.S. Patent No. 6,344,358), filed on March 28, 1999, which are hereby incorporated by reference in their entirety.

Please delete the following text beginning at page 62, line 20:

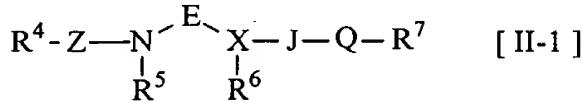
[This invention is based on application No. 09/321,745 filed in the United States of America, the content of which is incorporated hereinto by reference.]

IN THE CLAIMS

Cancel Claims 1-3, 9-12, 23-26, and 29-30.

Please amend claims as follows:

4. (Amended) [The] An agent for expression of long-term potentiation of synaptic transmission [of claim 1 or claim 2, wherein the] comprising a compound [has] having the following formula [II-1]:



wherein

R^4 is acyl,

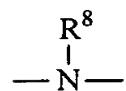
R^7 is lower alkyl, lower alkoxy, lower alkylamino, lower alkenyl, lower alkenyloxy, lower alkenylamino, lower alkynyl, lower alkynyloxy, lower alkynylamino, cyclo(lower)alkyl, cyclo(lower)alkyloxy, cyclo(lower)alkylamino, aryl, aryloxy, arylamino, a heterocyclic group or amino substituted with a heterocyclic group, each of which may be substituted with suitable substituent(s); or acyl;

Z is a single bond, $-CO-$ or $-SO_2-$,

E is lower alkylene optionally substituted with suitable substituent(s),

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl, substituted-lower alkyl, an N-protective group, aryl, acyl or a heterocyclic group,

Q is $-CH_2-$, $-CO-$, $-SO_2-$ or $-N=CH-$, and

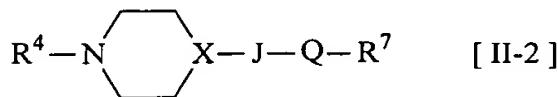
R^5 and R^6 are each hydrogen [or], lower alkyl, [or] are taken together to form lower alkylene [optionally] or are taken together to form lower alkylene condensed with a cyclic hydrocarbon or a heterocyclic ring,

provided that when X is N,

then 1) J is a single bond, and Q is $-CH_2-$, $-CO-$ or $-SO_2-$, or
2) J is lower alkylene,

or pharmaceutically acceptable salts thereof.

5. (Amended) [The] An agent for expression of long-term potentiation of synaptic transmission [of claim 1 or claim 2, wherein the] comprising a compound [has] having the following formula [II-2]:



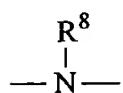
wherein

R^4 is acyl,

R^7 is aryl, aryloxy or arylamino, the aryl moiety of all of which may be substituted with halogen; pyridyl; or pyridylamino;

X is CH or N,

J is a single bond, lower alkylene or



wherein R^8 is hydrogen, lower alkyl or an N-protective group,

Q is $-CH_2-$, $-CO-$ or $-SO_2-$,

provided that when X is N, then J is a single bond or lower alkylene,

or pharmaceutically acceptable salts thereof.

6. (Amended) The agent for expression of long-term potentiation of synaptic transmission of [any of claim 1 to claim 5] claim 4, which is an agent for the prophylaxis or treatment of one or more cerebral diseases.

7. (Amended) The agent for expression of long-term potentiation of synaptic transmission of claim 6, [which is an agent for the prophylaxis or treatment of] wherein said cerebral disease is dementia or amnesia.

8. (Amended) A method for expressing long-term potentiation of synaptic transmission, comprising administering to a patient in need thereof an effective amount of a compound according to claim 4 [having a brain somatostatin activation property].

13. (Amended) The method for expressing long-term potentiation of synaptic transmission of [any of claim 8 to claim 12] claim 8, which is a method for the prophylaxis or treatment of one or more cerebral diseases.

14. (Amended) The method for expressing long-term potentiation of synaptic transmission of claim 13, [which is an agent for the prophylaxis or treatment of] wherein said cerebral disease is dementia or amnesia.

22. (Amended) A pharmaceutical composition for expression of long-term potentiation of synaptic transmission, which comprises a compound [having a brain somatostatin activation property,] according to claim 4 and a pharmaceutically acceptable carrier or excipient.

27. (Amended) The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of [any of claim 22 to claim 26] claim 22, which is a pharmaceutical composition for the prophylaxis or treatment of one or more cerebral diseases.

28. (Amended) The pharmaceutical composition for expression of long-term potentiation of synaptic transmission of claim 27, [which is an agent for the prophylaxis or treatment of] wherein said cerebral disease is dementia or amnesia.

31. (Amended) A method for screening an agent for expression of long-term potentiation of synaptic transmission, which comprises stimulating hippocampal slices, bringing a hippocampal slice into contact with a test compound of claim 4, measuring an amount of somatostatin released from the hippocampal slice and/or a release time thereof, measuring an amount of somatostatin released from a hippocampal slice and/or a release time thereof in the absence of a contact with the test compound, and comparing the amounts and/or the times to calculate the amount of somatostatin released from the hippocampal slice and/or the release time thereof caused by the contact with the test compound.

33. (Amended) [The] An agent for expression of long-term potentiation of synaptic transmission [of claim 1], wherein the compound having the brain somatostatin activation property is a compound obtained by the screening method of [any of claim 29 to claim 32] claim 31.

34. (Amended) [The] A method for expressing long-term potentiation of synaptic transmission [according to claim 8], comprising administering to a patient in need thereof an effective amount of a compound [, wherein the compound having the brain somatostatin activation property is a compound] obtained by the screening method of [any of claim 29 to claim 32] claim 31.

36. (Amended) [The] A pharmaceutical composition for expression of long-term potentiation of synaptic transmission [of claim 22, wherein the compound having the brain somatostatin activation property is] which comprises a compound obtained by the screening method of [any of claim 29 to claim 32] claim 31 and a pharmaceutically acceptable carrier or excipient.

37. (Amended) A commercial package comprising the pharmaceutical composition for expression of long-term potentiation of synaptic transmission of [any of] claim 22 [to claim 28 or claim 36] and a written matter associated therewith, wherein the written matter states that the pharmaceutical composition can or should be used for expression of long-term potentiation of synaptic transmission.

38. (Amended) A compound selected by the screening method [described in any] of claim [29 to claim 32] 31.

-- 39. – 54. (New) --



OSMM&N-File No. 215869US0PCT

Dept.: FF

By: NFO/dd

Serial No. 09/926,641

In the matter of the Application of: Nobuya MATSUOKA, et al.

For: AGENT FOR EXPRESSION OF LONG-TERM POTENTIATION OF
SYNAPTIC TRANSMISSION COMPRISING COMPOUND HAVING BRAIN
SOMATOSTATIN ACTIVATION PROPERTY

The following has been received in the U.S. Patent Office on the date stamped hereon:

pp. Specification Claims/Drawings Sheets
and Pages Application Data Sheet

Combined Declaration, Petition & Power of Attorney pages

List of Inventor Names and Addresses

Utility Patent Application Transmittal CPA

Notice of Priority Priority Doc

Check for Dep. Acct. Order Form

Fee Transmittal Form

Assignment/PTO 1595 pages:

Letter to Official Draftsman

Letter Requesting Approval of Drawing Changes

Drawings sheets Formal

Letter

Preliminary Amendment PTO-1449

Information Disclosure Statement Cited References

Search Report Statement of Relevancy Cited Pending Applications

IDS/Related/List of Related Cases Restriction Response Election Response

Restriction Response

Issue Fee Transmittal

White Advance Serial Number Card

Due Date: none

COPY

Rec'd PCT/PTO 14 MAR 2002



OSMM&N File No. 215869US0PCT By NFO/dd Due Date 11-28-01

Serial No. New U.S. PCT Application based on PCT/JP00/03334

In the matter of the Application of Nobuya MATSUOKA et al.

For AGENT FOR EXPRESSION OF LONG-TERM POTENTIATION OF
SYNAPTIC TRANSMISSION COMPRISING COMPOUND HAVING BRAIN
SOMATOSTATIN ACTIVATION PROPERTY

The following has been received in the U.S. Patent Office on the date stamped hereon:

pgs. Specification Claims (English Translation) pgs. Sequence Listing
 Combined Declaration, Petition & Power of Attorney (3 pages)
 Petition to Revive Under 37 C.F.R. 1.137 (b)
 Notice of Priority Under 35 U.S.C 120;
 Check for \$ 890.00; Dep. Acct. Order Form
 Assignment pages/PTO-1595
 Drawings sheets
 PCT Transmittal Letter
 Preliminary Amendment
 PCT/IB/304 PCT/IB/308
 Letter Regarding Claim to Small Entity Status
 International Preliminary Examination Report
 Information Disclosure Statement; PTO-1449
 Cite References () Statement of Relevancy
 List of Related Cases Cited Pending Applications(#)
 International Search Report
 Request for Consideration of Documents Cited in International Search Report
 Letter Regarding Translation of Annexes
 Translation of Annexes to International Preliminary Examination Report
Amended Sheets ()

SERIAL NO. **09/926641**

DATE RECEIVED **98 Rec'd PCT/PTO 28 NOV 2001**

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